

## REMARKS

Claims 1, 4-8, and 12-16 have been canceled without prejudice or disclaimer. Claims 18-36 have been added and therefore are pending in the present application. Claims 18-36 are supported throughout the specification, including the original claims.

The specification has been amended to update and to correct a typographical error in the Cross-Reference to Related Applications section.

Applicants enclose a substitute Declaration and Power of Attorney signed by the inventors.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

### I. The Rejection of Claims 1, 4-8, and 12-16 under 35 U.S.C. 103

Claims 1, 4-8, and 12-16 are rejected under 35 U.S.C. 103 as being unpatentable in view of Weigel *et al.* (WO 99/23227) in view of Kanani *et al.* (U.S. Patent No. 3,878,093). This rejection is respectfully traversed.

Weigel *et al.* disclose recombinant methods of producing hyaluronic acid in a *Bacillus* cell. Moreover, Weigel *et al.* disclose that cells can be separated from a fermentation broth by the addition of trichloroacetic acid to flocculate the cells and associated debris (page 63, lines 17-23).

However, Weigel *et al.* do not teach or suggest the addition of a divalent salt as a flocculating agent to a fermentation broth to flocculate *Bacillus* cells. Moreover, Weigel *et al.* do not teach or suggest adjusting the pH of the fermentation broth to a pH between 7.5 and 8.5. It is well known to persons of ordinary skill in the art that trichloroacetic acid would result in the fermentation broth becoming very acidic. Thus, Weigel *et al.* teach away from Applicants' claimed process.

Kanani *et al.* disclose a method for separating bacterial cells from an aqueous medium followed by flocculating the cells. The separation of the bacterial cells is achieved by subjecting the medium to at least one of the steps of (A) raising the pH of the medium to a value within the range 8 to 11 by treatment with an alkali, and (B) heating the medium to a temperature within the range 50°C to 200°C. The flocculation of the bacterial cells is achieved by lowering the pH to a value within the range of 2 to 5 by treatment with an acid, and separating the flocculated cells from the medium. Kanani *et al.* also teach that when the alkali treatment of step (A) is employed for the separating the bacterial cells from the aqueous medium, the pH is preferably

raised to a value within the range 8 to 9, but if the heating treatment of step (B) is omitted, a higher pH is preferred, e.g., 9 to 11. For raising the pH within the range 9 to 11, Kanani *et al.* disclose that sodium hydroxide is preferred, but other alkaline compounds may be used including potassium hydroxide and calcium hydroxide.

However, Kanani *et al.* do not teach or suggest the addition of a divalent salt as a flocculating agent to a fermentation broth to flocculate *Bacillus* cells. As mentioned above, Kanani *et al.* disclose that steps (A) and (B) do not achieve flocculation. For example in Example 1, Kanani *et al.* disclose the pH of a suspension of a *Pseudomonas methylotropha* strain was raised to 8.5. This step corresponds to step (A). Kanani *et al.* then reduce the pH to "3.5 by addition of sulphuric acid causing flocculation of the cells." Thus, Kanani *et al.* do not teach or suggest that a divalent salt such as a calcium salt is a flocculation agent.

The Office also relies on Wang et al. (Fermentation and Enzyme Technology, John Wiley and Sons, 1979, pp. 256-260) as support for "add[ing] calcium chloride and sodium hydroxide to fermentation broths to induce flocculation (see "12.3.1 Whole Cells", p. 257, for example). The functional ingredient for inducing flocculation is, in fact, calcium hydroxide." This is respectfully traversed.

Wang et al. expressly disclose at the top of page 257 that "Inorganic ions cannot cause flocculation although they may be used to neutralize charge and assist flocculation." Applicants therefore submit that Wang et al. teach away from using a divalent salt as a flocculating agent.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

## II. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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